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(54) Title: THROMBIN OR FACTOR Xa INHIBITORS

(57) Abstract: This invention relates generally to heteroaryl-phenyl substituted compounds that are inhibitors of trypsin-like serine protease enzymes, especially factor Xa or thrombin, pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

TITLE

Thrombin or Factor Xa Inhibitors

FIELD OF THE INVENTION

This invention relates generally to heteroaryl-phenyl substituted compounds that are inhibitors of trypsin-like serine protease enzymes, especially factor Xa or thrombin, pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

BACKGROUND OF THE INVENTION

Activated factor Xa, whose major practical role is the generation of thrombin by the limited proteolysis of prothrombin, holds a central position that links the intrinsic and extrinsic activation mechanisms in the final common pathway of blood coagulation. The generation of thrombin, the final serine protease in the pathway to generate a fibrin clot, from its precursor is amplified by formation of prothrombinase complex (factor Xa, factor V, Ca^{2+} and phospholipid). Since it is calculated that one molecule of factor Xa can generate 138 molecules of thrombin, inhibition of factor Xa may be more efficient than inactivation of thrombin in interrupting the blood coagulation system.

Therefore, efficacious and specific inhibitors of factor Xa, thrombin, or both are needed as potentially valuable therapeutic agents for the treatment of thromboembolic disorders. It is thus desirable to discover new factor Xa, thrombin, or both inhibitors.

SUMMARY OF THE INVENTION

Accordingly, one object of the present invention is to provide novel heteroaryl-phenyl substituted compounds that are useful as factor Xa inhibitors or pharmaceutically acceptable salts or prodrugs thereof.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

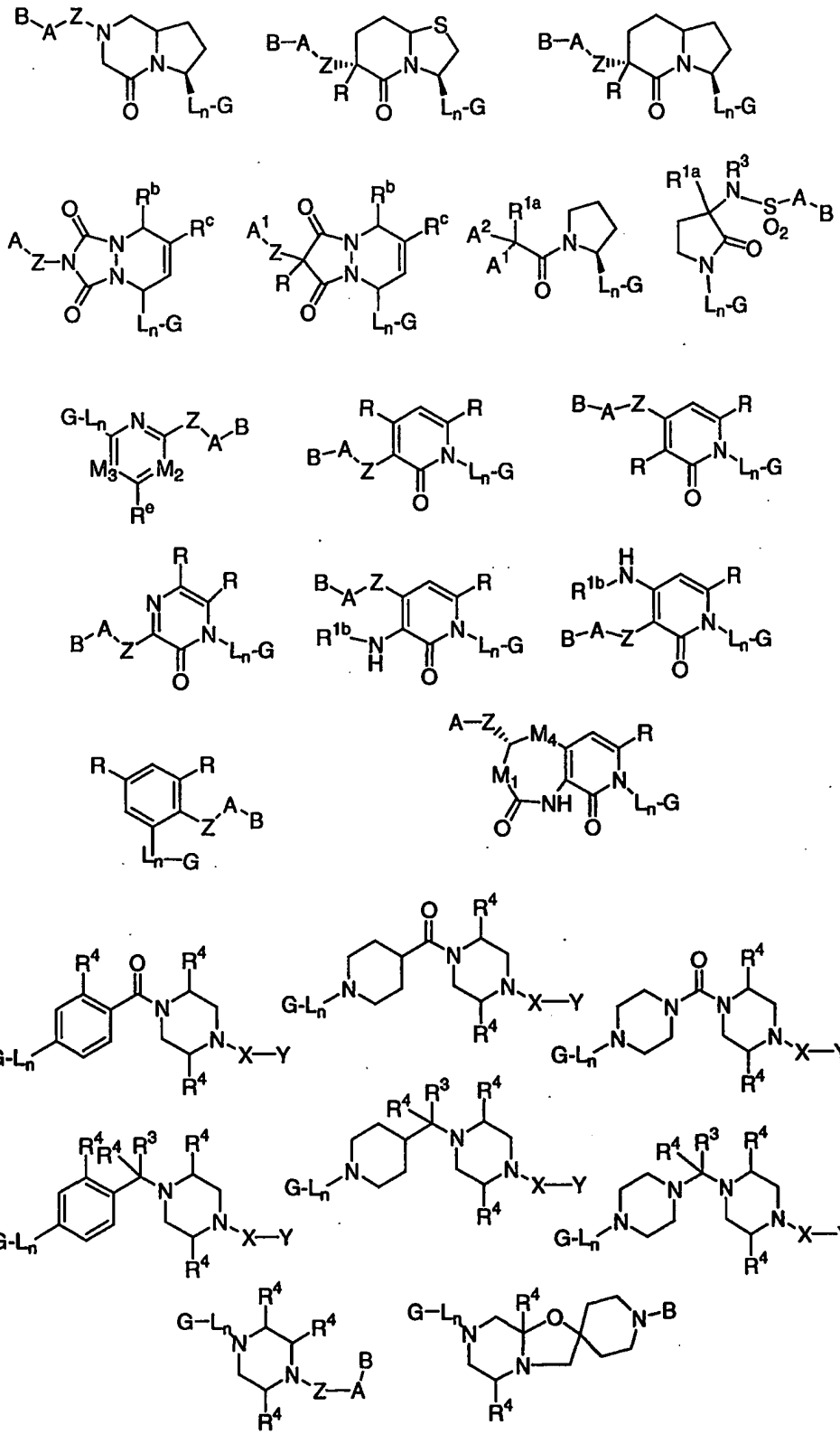
It is another object of the present invention to provide a method for treating thromboembolic disorders comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

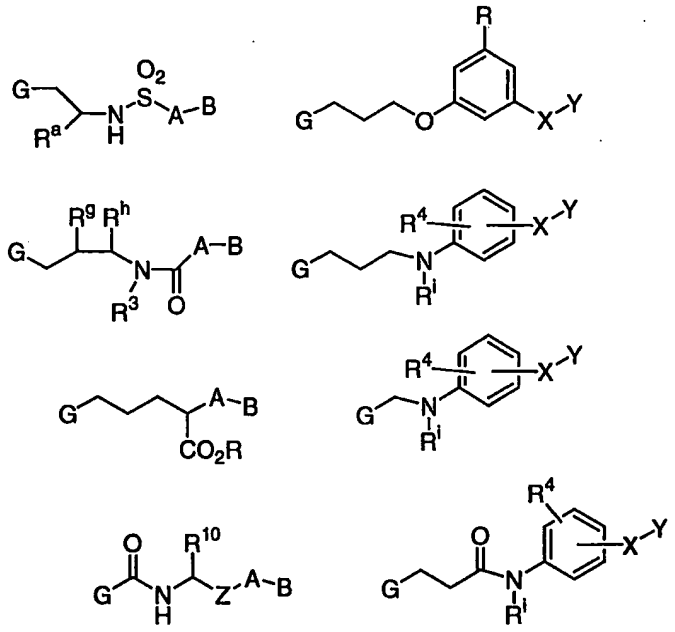
It is another object of the present invention to provide novel compounds for use in therapy.

It is another object of the present invention to provide the use of novel compounds for the manufacture of a medicament for the treatment of thrombosis or a disease mediated by factor Xa.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

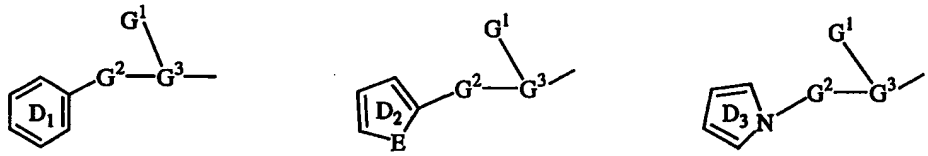
[1] Thus, in an embodiment, the present invention provides a novel compound selected from the group:





or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

G is selected from formulas Ia-Ic:



Ia Ib Ic

ring D_1 is selected from pyridine, pyrazine, pyridazine, and pyrimidine and is substituted with 1 D_{1a} and 0-1 D_{1b};

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-3 N atoms, wherein E is selected from O, S, and N-D_{1c} and ring D_2 is substituted with 1 D_{1a} and 0-1 D_{1b};

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 D_{1a} and 0-1 D_{1b};

G^1 is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

D_{1a} is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

D_{1b} is selected from H, C_{1-4} alkyl, F, Cl, Br, I, OH, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, CN, $C(=NR^8)NR^7R^9$, $NHC(=NR^8)NR^7R^9$, $NR^8CH(=NR^7)$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

D_{1c} is selected from H, C_{1-4} alkyl, OCH_3, OCH_2CH_3, $OCH(CH_3)_2$, $OCH_2CH_2CH_3$, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, $C(=NH)NH_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), $CH_2CH_2N(C_{1-3}$ alkyl)$_2$, $(CR^8R^9)_tNR^7R^8$, $(CR^8R^9)_tC(O)NR^7R^8$, and OCF_3;

G^2 is absent or is selected from CH_2, C(O), O, NR^3, $S(O)_p$, CH_2CH_2, $C(O)CH_2$, $CH_2C(O)$, OCH_2, CH_2O, NR^3CH_2, CH_2NR^3, $S(O)_pCH_2$, $CH_2S(O)_p$, $CH_2CH_2CH_2$, $C(O)CH_2CH_2$, $CH_2C(O)CH_2$, $CH_2CH_2C(O)$, OCH_2CH_2, CH_2OCH_2, CH_2CH_2O, $NR^3CH_2CH_2$, $CH_2NR^3CH_2$, $CH_2CH_2NR^3$, $S(O)_pCH_2CH_2$, $CH_2S(O)_pCH_2$, and $CH_2CH_2S(O)_p$;

G^3 is phenyl, naphthyl, or a 5-10 membered heteroaryl consisting of carbon atoms and from 1-3 heteroatoms selected from N, O, and S;

L_n is a linker which is absent or is selected from O, S, $S(O)_2$, CH_2, *NHC(O), *C(O)NH, $*S(O)_2NH$, $*NHS(O)_2$, $*CH_2NHC(O)$, $*CH(R^a)NHC(O)$, $*CH_2NHC(O)CH_2$, and $*CH(R^a)NHC(O)CH_2$, provided that L_n and M do not form an O-N or S-N bond and the * indicates where L_n is bonded to G;

M^1 is absent or is selected from CHR, O, and NR^2;

M^2 is N or CR^f;

M^3 is N or CR^d;

provided that only one of M^2 and M^3 is N;

M^4 is selected from NR^2, CR^f, and C(O);

R^a is selected from $C(O)C(O)OR^3$, $C(O)C(O)NR^2R^{2a}$, and C(O)-A;

R^b is selected from H, R, phenyl, C_{1-10} alkyl, and C_{2-5} alkenyl;

R^c is selected from H and C_{1-6} alkyl;

alternatively, R^b and R^c together are $-(CH_2)_4-$;

R^d is selected from H, F, and Cl;

R^e is selected from H, $N(CH_3)(CH_2CO_2H)$ and S-(5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4);

alternatively, R^d and R^e combine to form $-NR^3-C(O)-C(R^{1g}R^3)-NR^3-$ or $-N=CR^2-NR^3-$;

R^f is selected from H, F, and Cl;

alternatively, R^e and R^f combine to form $-NR^3-C(R^{1g}R^3)-C(O)-NR^3-$ or $-NR^3-CR^2=N-$;

R^g is selected from H, CH_2OR^3, $CH_2C(O)OR^3$, C_{1-4} alkyl, $C(O)NH_2$, and NH_2;

R^h is selected from H, CH_2-phenyl, CH_2CH_2-phenyl, and CH=CH-phenyl;

R^i is selected from $SO_2CH_2C(O)OR^3$, $C(O)CH_2C(O)OR^3$, and $C(O)OR^3$;

R is selected from H, Cl, F, Br, I, $(CH_2)_tOR^3$, C_{1-4} alkyl, benzyl, OCF_3, CF_3, $C(O)NR^7R^8$, $(CH_2)_tNR^2SO_2$-C_{1-4} alkyl, and $(CR^8R^9)_tNR^7R^8$;

Z is selected from a $(CR^8R^9)_{1-4}$, $(CR^8R^9)_rO(CR^8R^9)_r$, $(CR^8R^9)_rNR^3(CR^8R^9)_r$, $(CR^8R^9)_rNR^3C(=CHR^8)(CR^8R^9)_r$, $(CR^8R^9)_rC(O)(CR^8R^9)_r$, $(CR^8R^9)_rC(O)O(CR^8R^9)_r$, $(CR^8R^9)_rOC(O)(CR^8R^9)_r$, $(CR^8R^9)_rC(O)NR^3(CR^8R^9)_r$, $(CR^8R^9)_rNR^3C(O)(CR^8R^9)_r$, $(CR^8R^9)_rOC(O)O(CR^8R^9)_r$, $(CH_2)_rOC(O)NR^3(CR^8R^9)_r$, $(CR^8R^9)_rNR^3C(O)O(CR^8R^9)_r$, $(CH_2)_rNR^3C(O)NR^3(CR^8R^9)_r$, $(CR^8R^9)_rS(O)_p(CR^8R^9)_r$, $(CR^8R^9)_rS(O)_2(CH=CH)$, $(CCR^8R^9)_rSO_2NR^3(CR^8R^9)_r$, $(CR^8R^9)_rNR^3SO_2(CR^8R^9)_r$, and $(CR^8R^9)_rNR^3SO_2NR^3(CR^8R^9)_r$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with the groups to which Z is attached;

R^{1a} is selected from H, $-(CH_2)_r-R^{1b}$, $-CH=CH-R^{1b}$, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $NH(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, $S(O)_p(CH_2)_rR^{1d}$, $O(CH_2)_rR^{1d}$, $NR^3(CH_2)_rR^{1d}$, $OC(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)NR^3(CH_2)_rR^{1d}$, $NR^3C(O)O(CH_2)_rR^{1d}$, and $NR^3C(O)(CH_2)_rR^{1d}$, provided that R^{1a} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

R^{1b} is selected from H, C_{1-3} alkyl, F, Cl, Br, I, -CN, -CHO, $(CF_2)_rCF_3$, $(CH_2)_rOR^2$, NR^2R^{2a}, $C(O)R^{2c}$, $OC(O)R^2$, $(CF_2)_rCO_2R^{2a}$, $S(O)_pR^{2b}$, $NR^2(CH_2)_rOR^2$, $C(=NR^{2c})NR^2R^{2a}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NHR^{2b}$, $NR^2C(O)_2R^{2a}$, $OC(O)NR^{2a}R^{2b}$, $C(O)NR^2R^{2a}$, $C(O)NR^2(CH_2)_rOR^2$, $SO_2NR^2R^{2a}$, $NR^2SO_2R^{2b}$, C_{3-6}

carbocycle substituted with 0-2 R^{4a}, and 5-10 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1b} forms other than an N-halo, N-N, N-S, N-O, or N-CN bond;

R^{1c} is selected from H, $CH(CH_2OR^2)_2$, $C(O)R^{2c}$, $C(O)NR^2R^{2a}$, $S(O)R^{2b}$, $S(O)_2R^{2b}$, and $SO_2NR^2R^{2a}$;

R^{1d} is selected from C_{3-13} carbocycle substituted with 0-2 R^{4a}, and 5-13 membered heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-2 R^{4a}, provided that R^{1d} forms other than an N-N, N-S, or N-O bond;

R^{1g} is selected from H, C_{1-6} alkyl, and C_{1-6} alkyl substituted with A;

R^2, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2a}, at each occurrence, is selected from H, CF_3, C_{1-6} alkyl, benzyl, C_{3-6} cycloalkylmethyl substituted with 0-2 R^{4b}, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system containing from 1-4

heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2b}, at each occurrence, is selected from CF_3, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2c}, at each occurrence, is selected from CF_3, OH, C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, C_{3-6} carbocyclic residue substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and containing from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3a}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3b}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3c}, at each occurrence, is selected from C_{1-4} alkyl, and phenyl;

R^{3d}, at each occurrence, is selected from H, C_{1-4} alkyl, C_{1-4} alkyl-phenyl, and $C(=O)R^{3c}$;

A is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^4, and

5-12 membered heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

A^1 is H or A;

alternatively, A and A^1 and the carbon to which they are attached combine to form fluorene;

A^2 is selected from H, A, and CHA^3A^4;

A^3 is selected from H, A, C_{1-4} alkyl, and $-(CH_2)_rNR^2R^{2a}$;

A^4 is H or A;

B is selected from: H, Y, and X-Y, provided that Z and B are attached to different atoms on A;

X is selected from $-(CR^2R^{2a})_{1-4}-$, $-CR^2(CR^2R^{2b})(CH_2)_t-$, $-C(O)-$, $-C(=NR^{1c})-$, $-CR^2(NR^{1c}R^2)-$, $-CR^2(OR^2)-$, $-CR^2(SR^2)-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-S-$, $-S(O)-$, $-S(O)_2-$, $-SCR^2R^{2a}-$, $-S(O)CR^2R^{2a}-$, $-S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S-$,

$-CR^2R^{2a}S(O)-$, $-CR^2R^{2a}S(O)_2-$, $-S(O)_2NR^2-$, $-NR^2S(O)_2-$, $-NR^2S(O)_2CR^2R^{2a}-$, $-CR^2R^{2a}S(O)_2NR^2-$, $-NR^2S(O)_2NR^2-$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)O-$, $-OC(O)NR^2-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

Y is selected from:

C_{3-10} carbocyclic residue substituted with 0-2 R^{4a}, and 5-12 membered heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

alternatively, Z-A-B combine to form S-C_{1-6} alkyl;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_rF$, $(CH_2)_rCl$, $(CH_2)_rBr$, $(CH_2)_rI$, C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $C(=NS(O)_2R^5)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $C(O)NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, $(CF_2)_rCF_3$, $(CH_2)_r$-CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$, $O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CF_2)_rCF_3$, $(CH_2)_r$-CF_3, $(CH_2)_r$-F, $(CH_2)_r$-Br, $(CH_2)_r$-Cl,

C_{1-4} alkyl, $(CH_2)_rCN$, $(CH_2)_rNO_2$, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $(CH_2)_rN{=}CHOR^3$, $C(O)NH(CH_2)_2NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5;

R^{4b}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^3$, $(CH_2)_r$-F, $(CH_2)_r$-Cl, $(CH_2)_r$-Br, $(CH_2)_r$-I, C_{1-4} alkyl, $(CH_2)_r$-CN, $(CH_2)_r$-NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CH_2)_rCF_3$, and $(CF_2)_rCF_3$;

R^5, at each occurrence, is selected from H, C_{1-6} alkyl, =O, $(CH_2)_rOR^3$, F, Cl, Br, I, -CN, NO_2, $(CH_2)_rNR^3R^{3a}$, $(CH_2)_rC(O)R^3$, $(CH_2)_rC(O)OR^{3c}$, $NR^3C(O)R^{3a}$, $C(O)NR^3R^{3a}$, $NR^3C(O)NR^3R^{3a}$, $CH(=NOR^{3d})$, $C(=NR^3)NR^3R^{3a}$, $NR^3C(=NR^3)NR^3R^{3a}$, $SO_2NR^3R^{3a}$, $NR^3SO_2NR^3R^{3a}$, NR^3SO_2-C_{1-4} alkyl, $NR^3SO_2CF_3$, NR^3SO_2-phenyl, $S(O)_pCF_3$, $S(O)_p$-C_{1-4} alkyl, $S(O)_p$-phenyl, $(CF_2)_rCF_3$, phenyl substituted with 0-2 R^6, naphthyl substituted with 0-2 R^6, and benzyl substituted with 0-2 R^6;

R^6, at each occurrence, is selected from H, OH, $(CH_2)_rOR^2$, halo, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2b}$, $NR^2C(O)R^{2b}$, $NR^2C(O)NR^2R^{2a}$, $C(=NH)NH_2$, $NHC(=NH)NH_2$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, and $NR^2SO_2C_{1-4}$ alkyl;

R^7, at each occurrence, is selected from H, OH, C_{1-4} alkoxycarbonyl, C_{6-10} aryloxy, C_{6-10} aryloxycarbonyl, C_{6-10} arylmethylcarbonyl, C_{1-4} alkylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{6-10} arylcarbonyloxy C_{1-4} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, phenylaminocarbonyl, and phenyl C_{1-4} alkoxycarbonyl;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl, and $(CH_2)_n$-phenyl;

alternatively, R^7 and R^8, when attached to the same nitrogen, combine to form a 5-6 membered heterocyclic ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and $S(O)_p$;

R^9, at each occurrence, is selected from H, C_{1-6} alkyl and $(CH_2)_n$-phenyl;

R^{10} is selected from H, phenyl substituted with 0-2 R^{4a}, and naphthyl substituted with 0-2 R^{4a};

n, at each occurrence, is selected from 0, 1, 2, and 3;

m, at each occurrence, is selected from 0, 1, and 2;

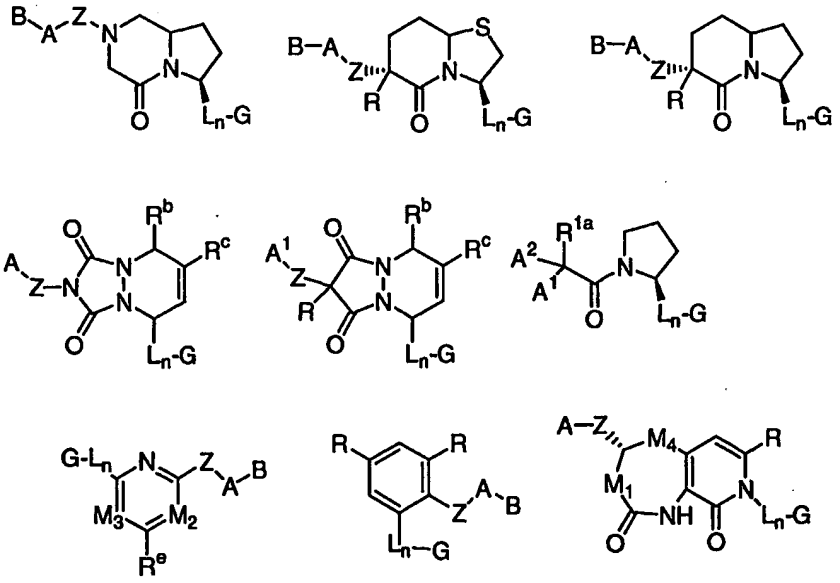
p, at each occurrence, is selected from 0, 1, and 2;

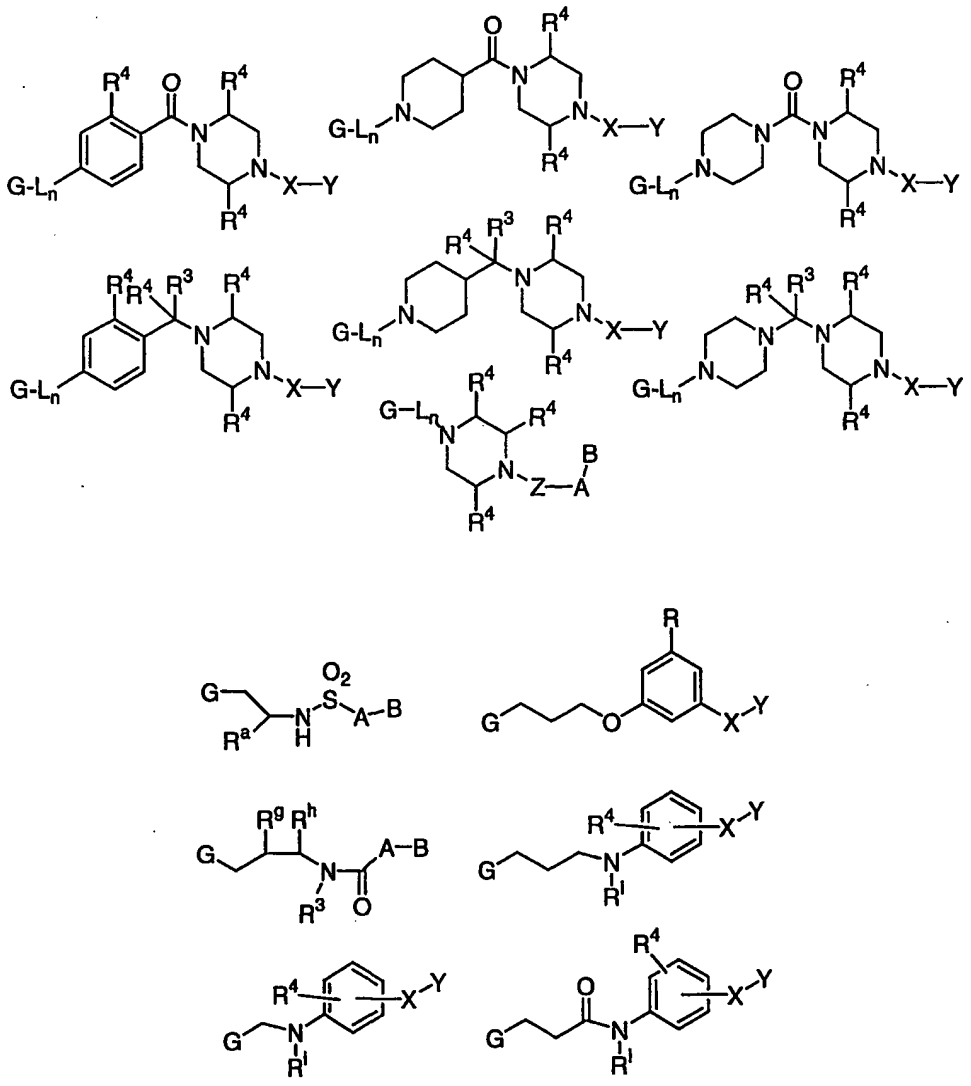
r, at each occurrence, is selected from 0, 1, 2, and 3;

s, at each occurrence, is selected from 0, 1, and 2; and,

t, at each occurrence, is selected from 0, 1, 2, and 3.

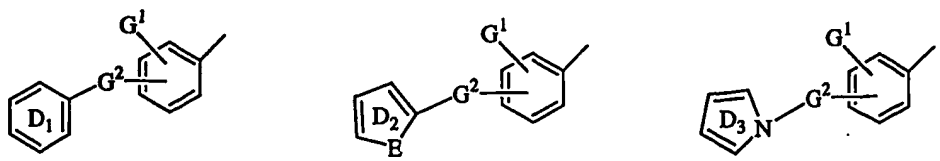
[2] Thus, in another embodiment, the present invention provides a novel compound selected from the group:





or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

G is selected from formulas Ia_1-Ic_1:



Ia_1 Ib_1 Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-D_{1c} and ring D_2 is substituted with 1 D_{1a} and 0-1 D_{1b};

ring D_3 is a 5-membered heteroaromatic ring system comprising carbon atoms and from 0-3 additional N atoms and ring D_3 is substituted with 1 D_{1a} and 0-1 D_{1b};

G^1 is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1a} is selected from H, OH, SH, C_{1-3} alkoxy, C_{1-3} thioalkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1b} is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1c} is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), $CH_2N(C_{1-3}$ alkyl)$_2$, $CH_2CH_2NH_2$, $CH_2CH_2NH(C_{1-3}$ alkyl), and $CH_2CH_2N(C_{1-3}$ alkyl)$_2$;

Z is selected from a bond, CH_2O, OCH_2, CH_2NH, $NHCH_2$, $NHC(=CH_2)$, $C(O)$, $CH_2C(O)$, $C(O)CH_2$, $NHC(O)$, $C(O)NH$, $NHC(O)NH$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, NCH_2N, or NCH_2O bond with ring M or group A;

A is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^4;

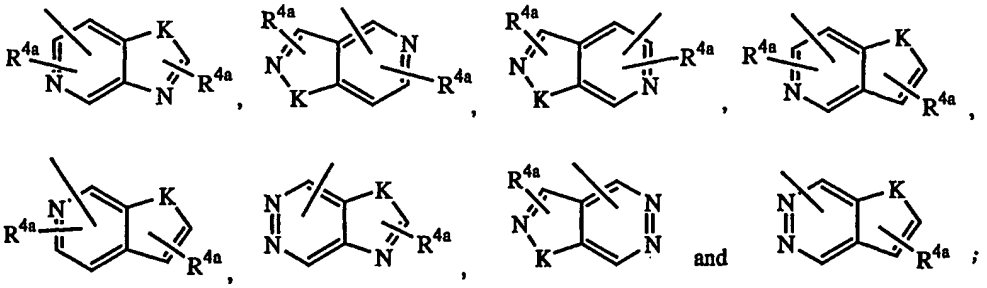
phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

X is selected from C_{1-4} alkylene, $-C(O)-$, $-C(=NR)-$, $-CR^2(NR^2R^{2a})-$, $-C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)$, $-C(O)NR^2-$, $-NR^2C(O)-$, $-C(O)NR^2CR^2R^{2a}-$, $-NR^2C(O)CR^2R^{2a}-$, $-CR^2R^{2a}C(O)NR^2-$, $-CR^2R^{2a}NR^2C(O)-$, $-NR^2C(O)NR^2-$, $-NR^2-$, $-NR^2CR^2R^{2a}-$, $-CR^2R^{2a}NR^2-$, O, $-CR^2R^{2a}O-$, and $-OCR^2R^{2a}-$;

alternatively, Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

cyclopropyl, cyclopentyl, cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, isoxazolinyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

alternatively, Y is selected from the following bicyclic heteroaryl ring systems:



K is selected from O, S, NH, and N;

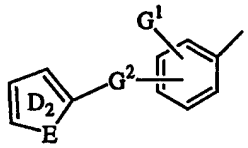
R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, NCH_2R^{1c}, OCH_2R^{1c}, SCH_2R^{1c}, $N(CH_2)_2(CH_2)_tR^{1b}$,

$O(CH_2)_2(CH_2)_tR^{1b}$, $S(CH_2)_2(CH_2)_tR^{1b}$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

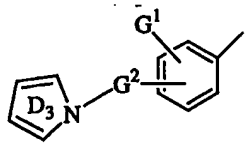
R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

[3] Thus, in another embodiment, the present invention provides a novel compound, wherein:

G is selected from formulas Ib_1 and Ic_1:



Ib_1



Ic_1

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-D_{1c} and ring D_2 is substituted with 1 D_{1a} and 0-1 D_{1b};

G^1 is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1a} is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1b} is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1c} is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

Y is selected from one of the following carbocyclic and heterocyclic systems which are substituted with 0-2 R^{4a};

phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thiophenyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazole, thiadiazole, triazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3-triazole, 1,2,4-triazole, 1,2,5-triazole, 1,3,4-triazole, benzofuran, benzothiofuran, indole, benzimidazole, benzimidazolone, benzoxazole, benzthiazole, indazole, benzisoxazole, benzisothiazole, and isoindazole;

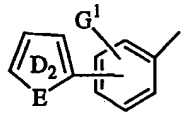
Z is selected from a bond, CH_2O, OCH_2, NH, CH_2NH, $NHCH_2$, $CH_2C(O)$, $C(O)CH_2$, $C(O)NH$, $NHC(O)$, $CH_2S(O)_2$, $S(O)_2(CH_2)$, SO_2NH, and $NHSO_2$, provided that Z does not form a N-N, N-O, N-S, NCH_2N, NCH_2O, or NCH_2S bond with either group to which it is attached;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $C(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $NR^2SO_2NR^2R^{2a}$, NR^2SO_2-C_{1-4} alkyl, $NR^2SO_2R^5$, $S(O)_pR^5$, CF_3, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5; and,

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, CF_3, F, Br, Cl, C_{1-4} alkyl, CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $NR^2C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $C(O)NHSO_2$-C_{1-4} alkyl, $S(O)_pR^5$, 5-6 membered carbocycle substituted with 0-1 R^5, and 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and $S(O)_p$ substituted with 0-1 R^5.

[4] In a preferred embodiment, the present invention provides a novel compound, wherein:

G is of formula Ib_2:



Ib_2

ring D_2 is a 5-membered heteroaromatic ring system comprising E, carbon atoms, and 0-2 N atoms, wherein E is selected from O, S, and N-D_{1c} and ring D_2 is substituted with 1 D_{1a} and 0-1 D_{1b};

G^1 is selected from H, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1a} is selected from H, OH, SH, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1b} is selected from H, C_{1-4} alkyl, Cl, F, Br, I, OH, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$;

D_{1c} is selected from H, C_{1-4} alkyl, C_{1-3} alkoxy, NH_2, $NH(C_{1-3}$ alkyl), $N(C_{1-3}$ alkyl)$_2$, CH_2NH_2, $CH_2NH(C_{1-3}$ alkyl), and $CH_2N(C_{1-3}$ alkyl)$_2$; and,

R is selected from H, Cl, F, Br, I, $(CH_2)_tOR^3$, C_{1-4} alkyl, OCF_3, CF_3, $C(O)NR^7R^8$, $(CR^8R^9)_tNR^7R^8$ and $(CH_2)_tNR^2SO_2$-CH_3.

[5] In a more preferred embodiment, the present invention provides a novel compound, wherein:

G is selected from the group:

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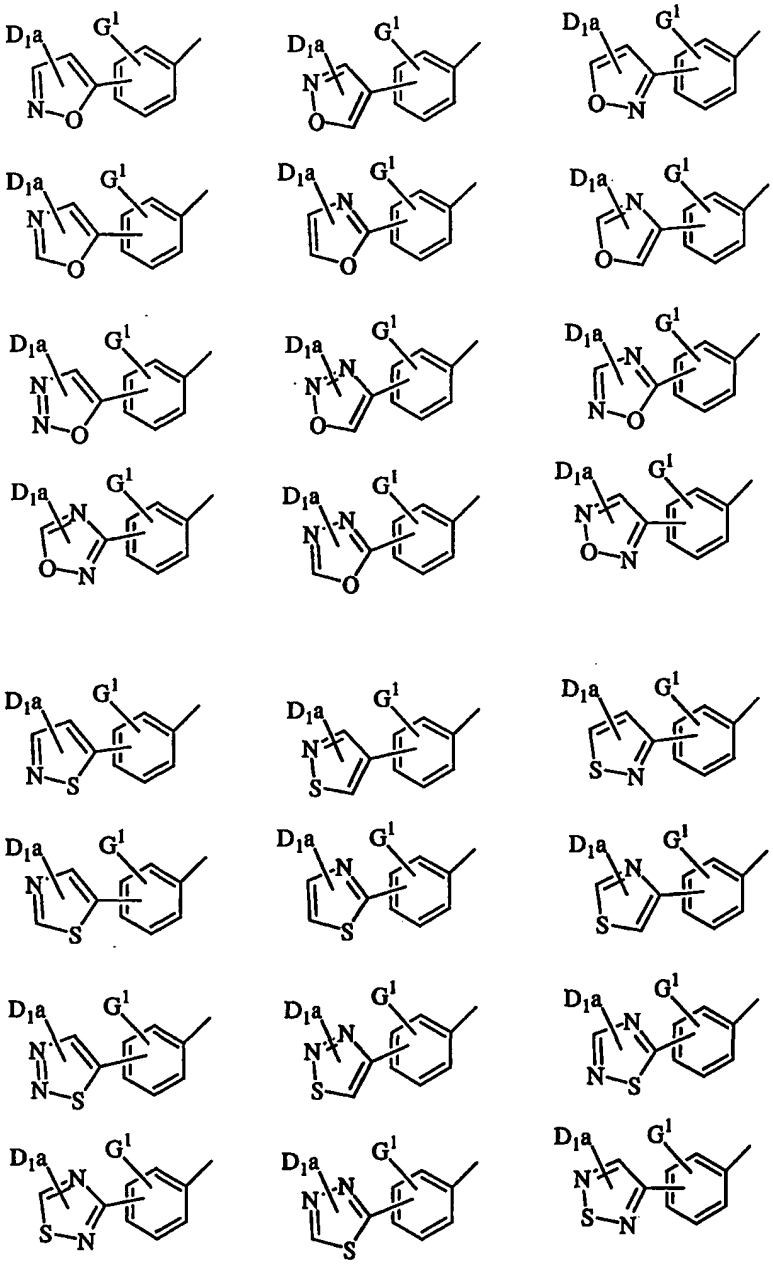
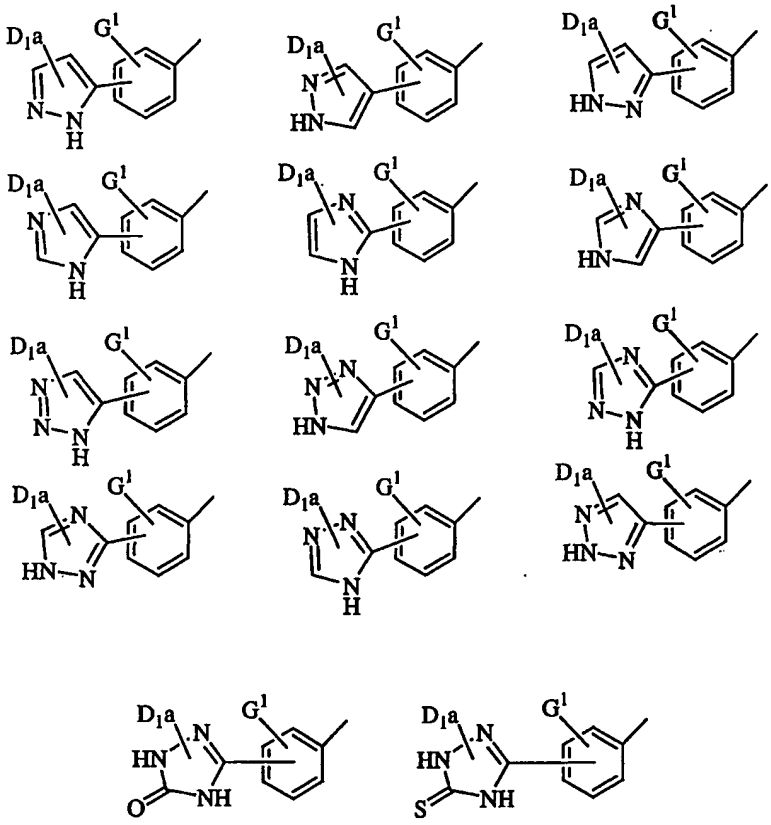




Z is selected from $C(O)CH_2$ and C(O)NH, provided that Z does not form a N-N bond with group A;

A is selected from phenyl, piperidinyl, pyridyl, and pyrimidyl, and is substituted with 0-2 R^4; and,

B is selected from phenyl, pyrrolidino, N-pyrrolidino-carbonyl, morpholino, N-morpholino-carbonyl, 1,2,3-triazolyl, imidazolyl, and benzimidazolyl, and is substituted with 0-1 R^{4a};

R^2, at each occurrence, is selected from H, CH_3, CH_2CH_3, cyclopropylmethyl, cyclobutyl, and cyclopentyl;

R^{2a}, at each occurrence, is selected from H, CH_3, and CH_2CH_3;

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form pyrrolidine substituted with 0-2 R^{4b} or piperidine substituted with 0-2 R^{4b};

R^4, at each occurrence, is selected from OH, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, F, Br, Cl, I, C_{1-4} alkyl, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, CF_3, and $(CF_2)CF_3$;

R^{4a} is selected from C_{1-4} alkyl, CF_3, OR^2, $(CH_2)OR^2$, $(CH_2)_2OR^2$, NR^2R^{2a}, $(CH_2)NR^2R^{2a}$, $(CH_2)_2NR^2R^{2a}$, SR^5, $S(O)R^5$, $S(O)_2R^5$, $SO_2NR^2R^{2a}$, and 1-CF_3-tetrazol-2-yl;

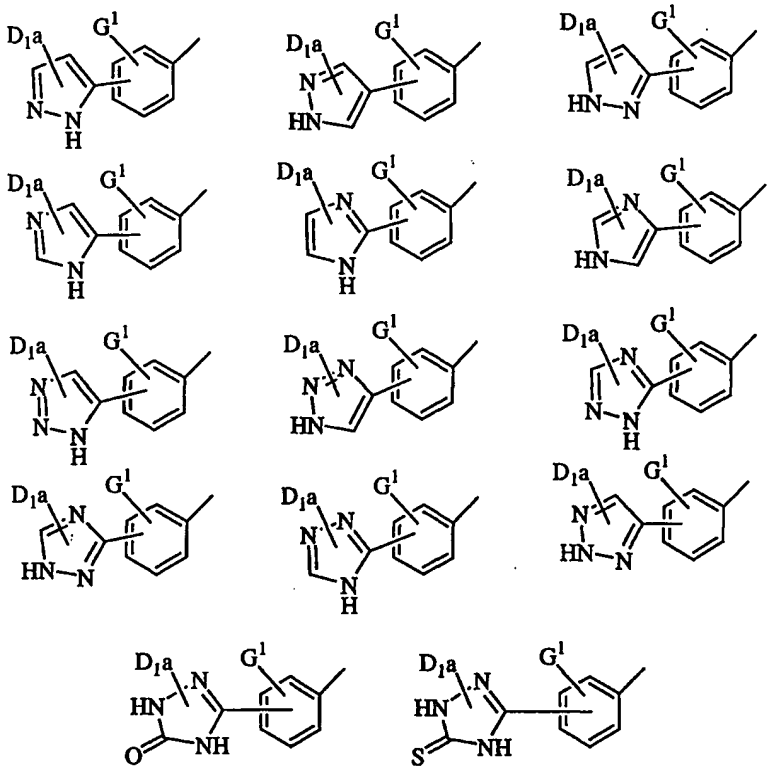
R^{4b}, at each occurrence, is selected from H, CH_3, and OH;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl; and,

r, at each occurrence, is selected from 0, 1, and 2.

[6] In an even further preferred embodiment, the present invention provides a novel compound, wherein:

G is selected from:

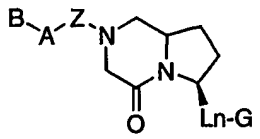


A is selected from the group: phenyl, piperidinyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl; and,

B is selected from the group: 2-(aminosulfonyl)phenyl, 2-(methylaminosulfonyl)phenyl, 1-pyrrolidinocarbonyl, 2-(methylsulfonyl)phenyl, 2-(N,N-dimethylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 2-(N-ethyl-N-methylaminomethyl)phenyl, 2-(N-pyrrolidinylmethyl)phenyl, 1-methyl-2-imidazolyl, 2-methyl-1-imidazolyl, 2-(dimethylaminomethyl)-1-imidazolyl, 2-(methylaminomethyl)-1-imidazolyl, 2-(N-(cyclopropylmethyl)aminomethyl)phenyl, 2-(N-(cyclobutyl)aminomethyl)phenyl, 2-(N-

(cyclopentyl)aminomethyl)phenyl, 2-(N-(4-hydroxypiperidinyl)methyl)phenyl, and 2-(N-(3-hydroxypyrrolidinyl)methyl)phenyl.

[7] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)CH_2$ or $*CH(R^a)NHC(O)CH_2$, the * indicates where L_n is bonded to G;

R^a is $C(O)C(O)OR^3$;

Z is selected from a C_{1-4} alkylene, $(CH_2)_rC(O)$, and $(CH_2)_rS(O)_2$;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2b}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is C_{5-6} carbocyclic residue substituted with 0-2 R^4;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl;

p, at each occurrence, is selected from 0, 1, and 2; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[8] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is $*CH(R^a)NHC(O)CH_2$;

R^a is $C(O)C(O)OH$;

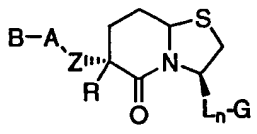
Z is selected from a CH_2, $(CH_2)_2C(O)$, and $CH_2S(O)_2$;

A is cyclohexyl or phenyl and is substituted with 0-1 R^4;

R^4, at each occurrence, is selected from H, =O, OR^2, CH_2OR^2, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, and 2.

[9] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)CH_2$ or $*CH(R^a)NHC(O)CH_2$, the * indicates where L_n is bonded to G;

R^a is $C(O)C(O)OR^3$;

R is H or NH_2;

Z is selected from a C_{1-4} alkylene, $(CH_2)_rC(O)$, and $(CH_2)_rS(O)_2$;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2b}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is a C_{5-6} carbocyclic residue substituted with 0-2 R^4;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl;

p, at each occurrence, is selected from 0, 1, and 2; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[10] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is $*CH(R^a)NHC(O)CH_2$;

R is H;

R^a is $C(O)C(O)OH$;

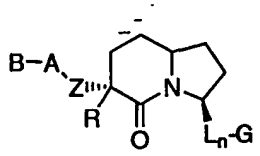
Z is selected from a CH_2, $(CH_2)_2C(O)$, and $CH_2S(O)_2$;

A is cyclohexyl or phenyl and is substituted with 0-1 R^4;

R^4, at each occurrence, is selected from H, =O, OR^2, CH_2OR^2, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

r, at each occurrence, is selected from 0, 1, 2, and 3.

[11] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)CH_2$ or $*CH(R^a)NHC(O)CH_2$, the * indicates where L_n is bonded to G;

R is H or NH_2;

R^a is $C(O)C(O)OR^3$;

Z is C_{1-4} alkylene;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2b}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is phenyl substituted with 0-2 R^4;

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl;

p, at each occurrence, is selected from 0, 1, and 2; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[12] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is $*CH(R^a)NHC(O)CH_2$;

R is NH_2;

R^a is C(O)C(O)OH;

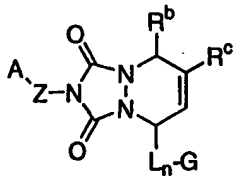
Z is CH_2;

A is phenyl substituted with 0-1 R^4;

R^4, at each occurrence, is selected from H, OR^2, CH_2OR^2, F, Cl, Br, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, and 2.

[13] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is *$CH_2NHC(O)$ or *$CH(R^a)NHC(O)$ and the * indicates where L_n is bonded to G;

R^a is selected from $C(O)C(O)OR^3$ and C(O)-A;

R^b is selected from H, phenyl, C_{1-10} alkyl, and C_{2-5} alkenyl;

R^c is selected from H and C_{1-6} alkyl;

alternatively, R^b and R^c together are $-(CH_2)_4-$;

Z is $(CR^8R^9)_{1-4}$;

R^2, at each occurrence, is selected from H, CF_3, and C_{1-6} alkyl;

R^{2a}, at each occurrence, is selected from H, CF_3, and C_{1-6} alkyl;

R^{2b}, at each occurrence, is selected from H, CF_3, and C_{1-6} alkyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is selected from:

C_{6-10} aromatic carbocyclic residue substituted with 0-2 R^4, and

5-10 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl and phenyl;

R^9, at each occurrence, is selected from H, C_{1-6} alkyl and phenyl;

p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3.

[14] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is *CH(R^a)NHC(O) and the * indicates where L_n is bonded to G;

R^a is C(O)C(O)OH or C(O)-(benzothiazol-2-yl);

R^b is selected from H, phenyl, C_{1-10} alkyl, and C_{2-5} alkenyl;

R^c is selected from H and C_{1-6} alkyl;

alternatively, R^b and R^c together are $-(CH_2)_4-$;

Z is $(CR^8H)_{1-2}$;

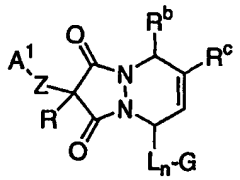
A is selected from phenyl, naphthyl, and thienyl, and A is substituted with 0-1 R^4;

R^4, at each occurrence, is selected from H, OR^2, CH_2OR^2, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

R^8, at each occurrence, is selected from H, methyl and phenyl; and,

r, at each occurrence, is selected from 0, 1, and 2.

[15] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)$ or $*CH(R^a)NHC(O)$ and the * indicates where L_n is bonded to G;

R^a is selected from $C(O)C(O)OR^3$ and C(O)-A;

R^b is selected from H, phenyl, C_{1-10} alkyl, and C_{2-5} alkenyl;

R^c is selected from H and C_{1-6} alkyl;

alternatively, R^b and R^c together are $-(CH_2)_4-$;

R is selected from H, benzyl, C_{1-4} alkyl, and NH_2;

Z is $(CR^8R^9)_{1-4}$;

R^2, at each occurrence, is selected from H, CF_3, and C_{1-6} alkyl;

R^{2a}, at each occurrence, is selected from H, CF_3, and C_{1-6} alkyl;

R^{2b}, at each occurrence, is selected from H, CF_3, and C_{1-6} alkyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is selected from:

C_{6-10} aromatic ring substituted with 0-2 R^4, and

5-10 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl and phenyl;

R^9, at each occurrence, is selected from H, C_{1-6} alkyl and phenyl;

p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3.

[16] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is *CH(R^a)NHC(O) and the * indicates where L_n is bonded to G;

R^a is C(O)C(O)OH or C(O)-(benzothiazol-2-yl);

R^b is selected from H, phenyl, C_{1-10} alkyl, and C_{2-5} alkenyl;

R^c is selected from H and C_{1-6} alkyl;

alternatively, R^b and R^c together are $-(CH_2)_4-$;

Z is $(CR^8H)_{1-2}$;

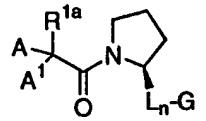
A is selected from phenyl, naphthyl, and thienyl, and A is substituted with 0-1 R^4;

R^4, at each occurrence, is selected from H, OR^2, CH_2OR^2, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl and phenyl;

r, at each occurrence, is selected from 0, 1, and 2.

[17] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)$ or $*CH(R^a)NHC(O)$ and the * indicates where L_n is bonded to G;

R^{1a} is selected from $-(CH_2)_r-R^{1b}$ and $NHCH_2R^{1c}$;

R^{1b} is selected from H, OR^2, NR^2R^{2a}, and $NR^2SO_2(CH_2)_rR^{2b}$;

R^{1c} is selected from $C(O)NR^2R^{2a}$, $S(O)_2R^{2b}$, and $SO_2NR^2R^{2a}$;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2b}, at each occurrence, is selected from C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, phenyl substituted with 0-2 R^{4b}, and 5-6 membered heterocyclic system containing from 1-2 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4b};

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R^{4b} and containing from 0-1 additional heteroatoms selected from the group consisting of N, O, and S;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is phenyl substituted with 0-2 R^4;

A^1 is H or A;

alternatively, A and A^1 and the carbon to which they are attached combine to form fluorene;

A^2 is selected from H, A, and CHA^3A^4;

A^3 is selected from H, A, C_{1-4} alkyl, and $-(CH_2)_rNR^2R^{2a}$;

A^4 is H or A;

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^{4b}, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl;

p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, and 3.

[18] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is $*CH_2NHC(O)$ and the * indicates where L_n is bonded to G;

R^{1a} is selected from $-(CH_2)_r-R^{1b}$ and $NHCH_2R^{1c}$;

R^{1b} is selected from OH, NR^2R^{2a}, and $NR^2SO_2(CH_2)_rR^{2b}$;

R^{1c} is selected from $C(O)NR^2R^{2a}$, $S(O)_2R^{2b}$, and $SO_2NR^2R^{2a}$;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2b}, at each occurrence, is selected from C_{1-4} alkoxy, C_{1-6} alkyl, benzyl, phenyl substituted with 0-1 R^{4b}, and pyrrolidinyl substituted with 0-1 R^{4b};

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

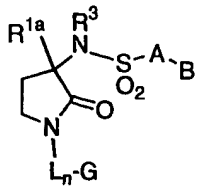
alternatively, R^2 and R^{2a}, together with the atom to which they are attached, combine to form a piperidine ring substituted with 0-1 R^{4b};

R^4, at each occurrence, is selected from H, =O, OR^2, CH_2OR^2, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

R^{4b}, at each occurrence, is selected from H, =O, OH, F, Cl, C_{1-4} alkyl, and NH_2; and,

r, at each occurrence, is selected from 0, 1, and 2.

[19] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is CH_2;

R^{1a} is $-(CH_2)_r-R^{1b}$;

R^{1b} is selected from H, C_{1-3} alkyl, $(CH_2)_rOR^2$, NR^2R^{2a}, $C(O)R^{2c}$, phenyl substituted with 0-2 R^4, and 5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2b}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is selected from:

C_{6-10} aromatic ring substituted with 0-2 R^4, and

5-10 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y

X is selected from C_{1-4} alkylene, $-NR^2-$, and O;

Y is selected from:

C_{6-10} aromatic ring substituted with 0-2 R^{4a}, and

5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^{4a}, at each occurrence, is selected from H, $(CH_2)_rOR^2$, Cl, Br, F, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, $S(O)_pR^5$, and CF_3;

R^5, at each occurrence, is selected from CF_3, C_{1-6} alkyl, phenyl, and benzyl;

p, at each occurrence, is selected from 0, 1, and 2; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[20] In another still more preferred embodiment, the present invention provides a compound wherein:

R^{1a} is $-(CH_2)_r-R^{1b}$;

R^{1b} is selected from H, C_{1-3} alkyl, OH, NR^2R^{2a}, and phenyl substituted with 0-2 R^4;

A is selected from:

phenyl substituted with 0-2 R^4, naphthyl substituted with 0-2 R^4, thienyl substituted with 0-2 R^4, benzothienyl substituted with 0-2 R^4, 5-aza-benzothienyl substituted with 0-2 R^4, 6-azabenzothienyl substituted with 0-2 R^4, and quinolinyl substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y

X is O;

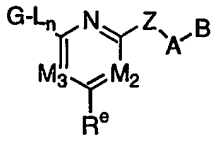
Y is phenyl substituted with 0-1 R^{4a};

R^4, at each occurrence, is selected from H, OR^2, CH_2OR^2, F, Cl, Br, I, C_{1-4} alkyl, -CN, $(CH_2)_rNR^2R^{2a}$, $C(O)NR^2R^{2a}$, and CF_3;

R^{4a}, at each occurrence, is selected from H, OR^2, CH_2OR^2, F, Cl, Br, I, C_{1-4} alkyl, -CN, $(CH_2)_rNR^2R^{2a}$, $C(O)NR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, and 2.

[21] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is O or S;

M^2 is N or CR^f;

M^3 is N or CR^d;

provided that only one of M^2 and M^3 is N;

R^e is selected from H, $N(CH_3)(CH_2CO_2H)$ and S-(5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4);

R^d is selected from H, F, and Cl;

alternatively, R^d and R^e combine to form $-NR^3-C(O)-C(R^{1g}R^3)-NR^3-$ or $-N=CR^2-NR^3-$;

R^f is selected from H, F, and Cl;

alternatively, R^e and R^f combine to form $-NR^3-C(R^{1g}R^3)-C(O)-NR^3-$ or $-NR^3-CR^2=N-$;

Z is O, provided that Z does not form a N-O or NCH_2O bond with the groups to which Z is attached;

R^{1g} is selected from H, C_{1-6} alkyl, and C_{1-6} alkyl substituted with A;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2b}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is selected from:

C_{5-6} carbocyclic residue substituted with 0-2 R^4, and

5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is H or Y;

Y is selected from:

C_{5-6} carbocyclic residue substituted with 0-2 R^{4a}, and

5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, $(CH_2)_r$-F, $(CH_2)_r$-Br, $(CH_2)_r$-Cl, Cl, Br, F, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $NR^2C(O)R^{2b}$, $C(O)NR^2R^{2a}$, $C(=NR^2)NR^2R^{2a}$, $NHC(=NR^2)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[22] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is O;

R^e is $N(CH_3)(CH_2CO_2H)$;

R^d is H or F;

alternatively, R^d and R^e combine to form $-NR^3-C(O)-C(R^{1g}R^3)-NR^3-$ or $-N=CR^2-NR^3-$;

R^f is H or F;

alternatively, R^e and R^f combine to form $-NR^3-C(R^{1g}R^3)-C(O)-NR^3-$ or $-NR^3-CR^2=N-$;

R^{1g} is selected from H, C_{1-2} alkyl and benzyl;

A is phenyl substituted with 0-2 R^4;

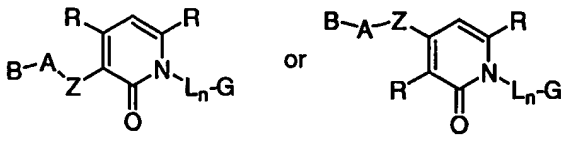
B is H or Y;

Y is 5 membered heterocyclic system containing from 1-2 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, C_{1-4} alkyl, and NR^2R^{2a}; and,

R^{4a}, at each occurrence, is selected from H, C_{1-4} alkyl, and NR^2R^{2a}.

[23] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)CH_2$ or $*CH(R^a)NHC(O)CH_2$ and the * indicates where L_n is bonded to G;

R^a is $C(O)C(O)OR^3$;

R, at each occurrence, is selected from H, Cl, F, Br, I, OR^3, C_{1-4} alkyl, $C(O)NH_2$, and NH_2;

Z is selected from a C_{1-4} alkylene and $(CH_2)_rSO_2NR^3$;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is selected from:

C_{5-6} carbocyclic residue substituted with 0-2 R^4, and

5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y

alternatively, when B is H, A is $(phenyl)_2CH$- substituted with 0-2 R^4;

X is selected from C_{1-4} alkylene, -C(O)-, $-NR^2-$, and O;

Y is selected from:

C_{5-6} carbocyclic residue substituted with 0-2 R^{4a}, and

5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, Cl, Br, F, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[24] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is $*CH_2NHC(O)CH_2$ and the * indicates where L_n is bonded to G;

R, at each occurrence, is selected from H and C_{1-4} alkyl;

Z is $CH_2SO_2NR^3$;

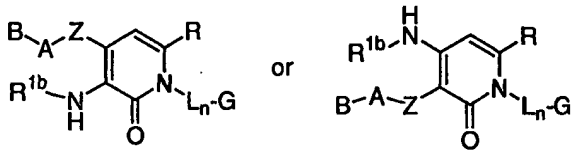
A is phenyl substituted with 0-2 R^4;

B is H;

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, C_{1-4} alkyl, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, and $C(O)NR^2R^{2a}$; and,

r, at each occurrence, is selected from 0, 1, and 2.

[25] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)CH_2$ or $*CH(R^a)NHC(O)CH_2$ and the * indicates where L_n is bonded to G;

R^a is $C(O)C(O)OR^3$;

R, at each occurrence, is selected from H, C_{1-4} alkyl, and NH_2;

R^{1g} is H or C_{1-6} alkyl;

Z is selected from a C_{1-4} alkylene and $(CH_2)_rS(O)_p(CH_2)_r$;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is selected from:

C_{3-6} carbocyclic residue substituted with 0-2 R^4, and

5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

B is selected from: H, Y, and X-Y

alternatively, when B is H, A is $(phenyl)_2CH$- substituted with 0-2 R^4;

X is selected from C_{1-4} alkylene, -C(O)-, $-NR^2-$, and O;

Y is selected from:

C_{5-6} carbocyclic residue substituted with 0-2 R^{4a}, and

5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

alternatively, Z-A-B combine to form S-C_{1-6} alkyl;

R^4, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, Cl, Br, F, I, C_{1-4} alkyl, -CN, NO_2, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

p is selected from 0, 1, and 2; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[26] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is $*CH_2NHC(O)CH_2$ and the * indicates where L_n is bonded to G;

R is H or C_{1-4} alkyl;

R^{1g} is H;

Z is CH_2, CH_2S, or $CH_2S(O)_2$;

A is a C_{3-6} carbocyclic residue substituted with 0-2 R^4;

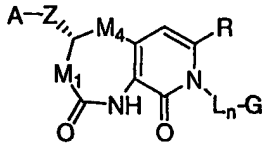
B is H

alternatively, Z-A-B combine to form $S-C_{1-6}$ alkyl;

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, C_{1-4} alkyl, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, and 2.

[27] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)CH_2$ or $*CH(R^a)NHC(O)CH_2$ and the * indicates where L_n is bonded to G;

M^1 is absent or is selected from CHR, O, and NR^2;

M^4 is selected from NR^2, CR^c, and C(O);

R is selected from H, Cl, F, Br, I, OR^3, C_{1-4} alkyl, OCF_3, CF_3, and NH_2;

Z is C_{1-4} alkylene;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

A is selected from:

C_{3-6} carbocyclic residue substituted with 0-2 R^4, and

5-6 membered aromatic heterocyclic system containing from 1-4 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^4;

R^4, at each occurrence, is selected from H, $(CH_2)_rOR^2$, F, Cl, Br, I, C_{1-4} alkyl, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[28] In another still more preferred embodiment, the present invention provides a compound wherein:

L_n is $*CH_2NHC(O)CH_2$ and the * indicates where L_n is bonded to G;

M^1 is absent;

R is selected from H and C_{1-4} alkyl;

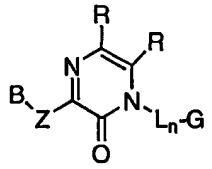
Z is CH_2;

A is C_{3-6} carbocyclic residue substituted with 0-1 R^4;

R^4, at each occurrence, is selected from H, C_{1-4} alkyl, $(CH_2)_rNR^2R^{2a}$, and CF_3; and,

r, at each occurrence, is selected from 0, 1, and 2.

[29] In another even more preferred embodiment, the present invention provides a compound of formula:



L_n is $*CH_2NHC(O)CH_2$ or $*CH(R^a)NHC(O)CH_2$ and the * indicates where L_n is bonded to G;

R^a is $C(O)C(O)OR^3$;

R, at each occurrence, is selected from H, Cl, F, Br, I, OR^3, C_{1-4} alkyl, $C(O)NH_2$, and NH_2;

Z is $(CHR^8)NR^3$, $(CHR^8)_2NR^3$, and $(CHR^8)_2SO_2R^3$;

provided that when Z is $(CHR^8)_2NR^3$, then B is absent;

R^2, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2a}, at each occurrence, is selected from H, C_{1-6} alkyl, benzyl, and phenyl;

R^{2c}, at each occurrence, is selected from OH, OCH_3, OCH_2CH_3, CH_3, benzyl, and phenyl;

R^3, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

R^{3a}, at each occurrence, is selected from H, C_{1-4} alkyl, and phenyl;

B is H or Y;

Y is selected from:

C_{5-6} carbocyclic residue substituted with 0-2 R^{4a}, and

5-6 membered heterocyclic system containing from 1-2 heteroatoms selected from the group consisting of N, O, and S substituted with 0-2 R^{4a};

R^{4a}, at each occurrence, is selected from H, =O, $(CH_2)_rOR^2$, Cl, Br, F, I, C_{1-4} alkyl, -CN, $(CH_2)_rNR^2R^{2a}$, $(CH_2)_rC(O)R^{2c}$, $C(O)NR^2R^{2a}$, $SO_2NR^2R^{2a}$, and CF_3;

R^8, at each occurrence, is selected from H, C_{1-6} alkyl and phenyl; and,

r, at each occurrence, is selected from 0, 1, 2, and 3.

[30] In another still more preferred embodiment, the present invention provides a compound wherein: